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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/489,088	01/21/2000	Sung-Yun Kwon	7010-0014	5348

22428 7590 04/21/2005

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/489,088	KWON ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 20-40* is/are pending in the application.

4a) Of the above claim(s) *33-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 20-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The receipt is acknowledged of applicants' response under 1.111, filed 09/22/2004.

Claims 1-18, and 20-40 are pending. Claims 33-40 are withdrawn from further consideration as being drawn to a nonelected Group II. Claims 1-18, and 20-32 are included in the prosecution.

Claim Rejections - 35 USC § 103

1. Claims 1-18, 20-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/29134 ('134) in view of US 5,630,796 ('796).

Claim 1 reads as a method for administering a therapeutic agent to the skin or mucosa comprising accelerating particles into or across the skin or mucosa using a needless syringe; and topically positioning a transdermal drug delivery device or occlusive dressing on the area of the skin or mucosa.

WO '134 teaches a method of enhancing the permeability of a permeant (active agent) across of a biological membrane including skin or mucosa utilizing microporation of the membrane at the site of administration, followed by contacting the porated surface by the active agent and a permeation enhancer (abstract; page 9, lines 5-10; page 10, line 8; page 15, line 14; page 19, lines 6-15; page 34, lines 5-9; page 100,

lines 14-16). The active agent includes polypeptide and vaccine associated with a carrier such as microcapsules or microparticles (page 14, lines 19-25; page 15, lines 1-4; page 29, line 11). The micropores should not be smaller than 1 micron in diameter (page 25, lines 3-4). The pores can be covered by transdermal patch to deliver the active agent through the skin (page 118, Example 50). The reference suggests forming the pores using any non-invasive means that do not require entry of needle to the skin or mucosa or invasive instruments (page 32, lines 10-11).

WO '134, however, does not teach the needleless syringe used to form the skin pores, but suggests forming the pores using any non-invasive means that do not require entry of needle to the skin or mucosa or invasive instruments.

US '796 teaches a noninvasive method comprising needleless syringe for effective transdermal delivery of particles containing a therapeutic agent. The needleless method provides safe quick method with less pain and no risk of infection. The active agents include viruses or proteins (antigen), insulin with a carrier (adjuvant) or a placebo. Injection velocities may be between 200 up to 3000 m/sec. and the particle size ranges from 0.1 to 250 micrometer. The particles can be made from metal. The drug particles can be encapsulated. More than one therapeutic agent can be injected together. See the abstract, col.1, lines 61-63; col.2, lines 30-37; col.4, lines 1-23, 40-55; col.8, lines 17-20; col.10, example 2.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to provide a method for administering a therapeutic agent to the skin or mucosa comprising forming pores in the skin or mucosa using

noninvasive means followed by topical application of the active agent by a patch as disclosed by WO '134, and use the noninvasive needleless syringe disclosed by US '796 to form the skin pores, motivated by the teaching of US '796 that the needleless method is safe quick method with less pain and no risk of infection, with reasonable expectation of having a method for delivery of active agents across the skin or mucosa comprising porating the skin with needleless syringe followed by application of a topical device such a method accelerates the drug delivery through the skin or mucosa to the systemic circulation safely and quickly with no pain.

Response to Arguments

2. Applicant's arguments filed 09/22/2004 have been fully considered but they are not persuasive.

Applicants traverse the obviousness rejection of claim 1-8 and 20-32 over WO '134 in view of US '796 by arguing that WO '134 teaches microporation that is carried out to form micropores of selected depth of the skin or mucosa, then connected to permeant and additionally an enhancer may be applied to enhance the flux of the permeant. WO '134 does not mention the use of particles administered via a needleless syringe wherein the fluid propel the particle, but mentioned the use of high pressure jet that puncture the biological membrane. WO '134 teaches that the poration of the membrane is followed by the application of a therapeutic agent.

In response to this argument, the examiner is pointing out to the scope of the present claims which is method for transdermal drug delivery comprising two steps, first

is accelerating particles into area of skin, and second is positioning a transdermal drug delivery device to the site the delivery of a therapeutic agent over that skin area; wherein the particle or the device or both can contain active agent or not, i.e. placebo. WO '134 teaches enhancing the trans-membrane (skin or mucosa) flux rate of a drug into a selected area achieved by minimally invasive or non-invasively making micropores to the membranes (abstract; page 7, lines 18-20). WO '134 defines "non-invasive" by: "means not requiring the entry of a needle". Therefore, the reference teaches non-invasive needleless formation of micropores, which is the method claimed by applicants. WO '134 used high pressure jet fluid to make the perforation for the same purpose desired by applicants, which is accelerate the delivery of the transdermal therapeutic agent that is applied subsequently from a transdermal delivery device. Therefore, WO '134 recognized method for transdermal drug delivery by making micropores to the skin using no needle, followed by application of a transdermal drug delivery device. The only difference between WO '134 and the present invention is WO '134 does not teach the use of particles and needleless syringe to make the micropores, which is taught by the secondary reference. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue that US '796 teaches membrane ruptures by gas pressure to supersonic gas flow in which particles containing the therapeutic agent are injected. US

'796 teaches away from combination with other method as it teaches method that it stands on its own as effective transdermal delivery method of therapeutic agent and therefore can not reasonably be expected to be used in multi step drug delivery technique.

In response to applicants' argument against US '796, as stated above WO '134 teaches method for trans-membrane delivery comprising the step of making micropores to that membrane using non-invasive needleless method, followed by administration of a transdermal device. However, WO '134 does not teach using particles from a syringe to make the micropores. US '796 is relied upon for teaching what is missing from WO '134 to arrive to the present invention, i.e. needleless syringe and particles that may contain the drug or just a placebo, col.10, line 56. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The test for obviousness is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Hence, WO '134 teaches the multi-step process to enhance delivery of active agent, first step of making micropores, and second step of applying transdermal device; and US '796 teaches a needleless painless method for making the micropores which at the same time can deliver active agents. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to provide a method for administering a therapeutic agent to the skin or mucosa comprising forming pores in the

skin or mucosa using noninvasive means followed by topical application of the active agent by a patch as disclosed by WO '134, and use the noninvasive needleless syringe disclosed by US '796 to form the skin pores, motivated by the teaching of US '796 that the needleless method is safe quick method with less pain and no risk of infection, with reasonable expectation of having a method for delivery of active agents across the skin or mucosa comprising porating the skin with needleless syringe followed by application of a topical device such a method accelerates the drug delivery through the skin or mucosa to the systemic circulation safely and quickly with no pain.

Absent some motivation to combine WO '134 and US '796, the examiner cannot make out a prima facie case of obviousness. The examiner has not provided any reasoning why one skilled in the art at the time of the invention would have been motivated to combine the method of needless delivery of a pharmaceutical agent disclosed by US '796 with a second method for subsequently administering the pharmaceutical agent at the same site through a topical patch.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, WO '134 teaches

the multi-step process to enhance delivery of active agent, first step of making micropores using non-invasive needleless method, and second step of applying transdermal device comprising the active agent; and US '796 is relied upon for teaching a needleless painless method for making the micropores which at the same time can deliver active agents. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to provide a method for administering a therapeutic agent to the skin or mucosa comprising forming pores in the skin or mucosa using noninvasive means followed by topical application of the active agent by a patch as disclosed by WO '134, and use the noninvasive needleless syringe that deliver particles to make the micropores as disclosed by US '796, motivated by the teaching of US '796 that the needleless method is safe quick method with less pain and no risk of infection that meanwhile could deliver active agent as it form the micropores, with reasonable expectation of having a method for delivery of active agents across the skin or mucosa comprising porating the skin with needleless syringe that deliver particles followed by application of a topical device such a method accelerates the drug delivery through the skin or mucosa to the systemic circulation safely and quickly with no pain. It is well established that the claims are given the broadest interpretation during examination. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969). In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined

by the claims would have been prima facie obvious over WO '134 in view of US '796 within the meaning of 35 U.S.C. 103 (a).

Neither reference suggests the multi-step drug delivery technique, nor do they suggest neither method is incomplete or ineffective. US '796 does not teach the placebo particles. No suggestion by US '796 of enhanced delivery of a subsequently delivered therapeutic as suggested by the examiner.

In response to this argument, the examiner is pointing out to the teaching of WO '134 that teaches the multi-step process to enhance delivery of active agent, first step of making micropores using needleless method, and second step of applying transdermal device; and US '796 is relied upon for teaching a needleless painless method for making the micropores using particles which at the same time can deliver active agents, wherein the method of forming micropores disclosed by US '796 can replace the first step of the method for transdermal delivery disclosed by WO 134. US '796 teaches the placebo particles can be delivered by the needleless syringe, col.10, line 56. US '796 is relied upon for teaching the needleless syringe that deliver particles to make micropores, and it does not need to teach the multi-step delivery method that is taught by WO '134. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972). The fact that applicant has recognized another advantage,

which is using placebo, which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

The examiner rewrote the prior art, ignoring the clear teaching from the art, and arrived at an entirely inconsistent and unsupportable position as a hallmark of an improper hindsight reconstruction of applicant's claimed invention.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In any event, WO '134 teaches the multi-step method for transdermal delivery of an active agent, and US '796 is relied upon for teaching an alternative method for making micropores to the skin that is safe and painless and also deliver active agents simultaneously.

The examiner's assertion that one skilled in the art would be motivated to combine the two references because US '796 teaches that the needleless method is "a safe and quick method with less pain and no risk of infection" is inapposite. US '796

does note that the "main advantages which flow from the invention include no needle and less pain, no risk of infection, delivery of drugs in natural solid form, quicker and safer to use than liquid drug, by syringe and needle and no sharps to dispose of."

In response to this argument, the examiner position is that in considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

However, nothing in either of the references suggests that the needless delivery method of US '796 would enhance the permeation of a subsequently administered therapeutic agent. Instead, US '796 clearly discloses that it is a method of delivering a therapeutic agent. The fact that the method is safe and quick, by itself, does not provide a motivation to combine the references. Accordingly, the Examiner's rationale does not

provide any motivation to combine the US '796 method with a second method of delivering a therapeutic agent as disclosed in WO '134.

In response to this argument, the examiner position is that the primary reference WO '134 teaches the multi-step process to enhance delivery of active agent, first step of making micropores using non-invasive needleless technique, and second step of applying transdermal device; and US '796 is relied upon for teaching a needleless painless method for making the micropores which can deliver active agents at the same time. US '796 teaches an alternative method for making microporation to the skin that can be applied into the method of WO '134. Again, in considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

Conclusion

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

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